The High-Risk TIA Patient: Part One—Diagnosis

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A transient ischemic attack (TIA) is a stroke warning event. As many as one in four ischemic strokes are preceded by a warning TIA, with 43% of TIAs occurring within one week before the stroke.[1] With increasing data emphasizing the dangers soon after a TIA, our clinical approach to such patients is necessarily becoming more aggressive. Accurate and rapid identification of high-risk TIA patients is essential to ensure optimal treatment decisions for stroke prevention. This article provides some pearls to aid in the diagnosis, prognosis, triage and treatment of patients with TIA, with updates from new guidelines and recent studies. Part one of this review focuses on diagnostic evaluation and part two discusses treatment issues. While the term TIA is used throughout, the same diagnostic and treatment strategies apply to patients with a minor ischemic stroke.

Meet Beatrice

- Beatrice, 65, presents with an acute onset of weakness and numbness of the right arm for 30 minutes. Her hand was clumsy and she was unable to put in her contact lenses
- Vascular risk factors include hypertension and hyperlipidemia. Her history is negative for diabetes, smoking, coronary artery disease and atrial fibrillation (AF)
- Examination is significant for BP 150/80 mmHg and a left carotid bruit
- Neurological examination is normal, apart from mild residual impairment in right hand dexterity
- CT brain scan is unremarkable, but a MRI scan reveals areas of restricted diffusion (Figure 1) in the sensorimotor cortex of the left cerebral hemisphere, indicating acute cerebral ischemia
- Carotid Doppler ultrasound demonstrates high-grade (85%) stenosis of the left internal carotid artery

For more info on Beatrice, turn to page 64...

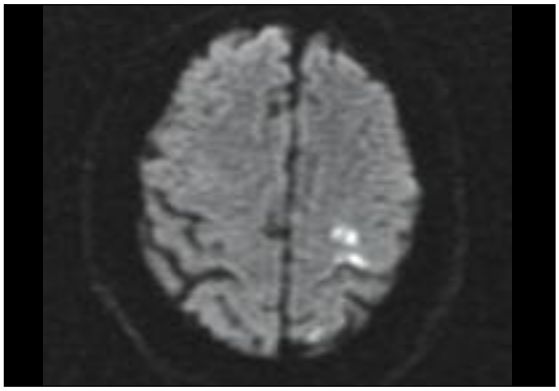

Figure 1. Diffusion-weighted brain MRI scan demonstrating areas of acute ischemia (bright signal abnormality) within the left sensorimotor cortex, caused by embolism from a ruptured atherosclerotic plaque within the ipsilateral internal carotid artery in the neck.

Early stroke risk after a TIA

Overall, patients with a TIA have a 15% to 20% risk of having a stroke within three months.[2-4] This risk is front-loaded, with half of strokes occurring within the first 48 hours post TIA.[3,5] When stratified by additional risk factors, some patients have a seven-day stroke risk of > 30%.

Features of a high-risk TIA

Clinical features associated with a higher risk of early stroke are motor TIA (sudden unilateral weakness) or speech TIA (sudden aphasia or dysarthria). The timing of the event is a key risk factor—an acute TIA poses a much higher risk

Table 1
ABCD^2 score for predicting early stroke risk following a transient ischemic attack (TIA)[7]

	Clinical variable	Scoring
A	Age	1 point for age > 60 years
B	BP	1 point for systolic BP > 140 mmHg or diastolic BP > 90 mmHg
C	Clinical features	2 points for sudden unilateral weakness 1 point for sudden speech disturbance without weakness
D	Duration of TIA symptoms	2 points for > 60 minutes 1 point for 10-59 minutes
D	Diabetes	1 point

Total score	0-3 points (lower risk)	4-5 points (moderate risk)	6-7 points (higher risk)
Predicted 2-day stroke risk	1%	4.1%	8.1%

than events occurring weeks or months earlier. Additional clinical variables associated with elevated risk include older age, diabetes, hypertension and a longer duration of TIA symptoms.[3,6] A new scale (the ABCD^2 score) has been proposed for clinical risk stratification (Table 1). Such scales may assist in triaging patients in the office or ED, or in selecting patients for extended observation or hospital admission. In contrast to cerebral hemispheric TIAs, a retinal TIA or amaurosis fugax (*i.e.*, sudden painless loss of vision in one eye) carries a lower risk of early recurrent events. Some patients have recurrent pure sensory spells that appear relatively benign and whether or not these represent true TIAs is not always clear. Ultimately, it is the underlying mechanism of ischemia that is the key to distinguishing high- vs. low-risk patients.

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Making the correct diagnosis

TIAs are frequently overdiagnosed in patients who report transient neurological symptoms. Therefore, accurate identification of a true TIA and distinguishing it from its many mimics, is always the first priority. Most TIA symptoms last less than one hour, so the diagnosis usually relies on a careful history from the patient (and ideally with corroboration by a witness) to avoid misdiagnosis or overdiagnosis. For pragmatic purposes, the authors find it useful to include descriptive terms to communicate risk, urgency and certainty of diagnosis of a cerebral ischemic event (*i.e.*, "possible" if the clinical history is not typical, "probable" if the history is suggestive and "definite" when there is imaging confirmation). Additionally, the timing of the event should be indicated as "acute," "recent," or "remote." The clinical symptoms (*e.g.*, a motor or speech TIA) should also be indicated to convey risk. For example, Beatrice presented with a definite, acute, motor TIA and therefore was considered high risk and triaged accordingly. In contrast, a patient with a "remote, possible, pure sensory TIA" might be classified as lower risk.

Common TIA mimics

Transient neurological symptoms that are unlikely to represent TIA include nonspecific dizzy spells, presyncope, syncope, generalized (rather than focal) weakness and nonspecific visual symptoms.

In a study of 1,297 patients presenting to hospital with isolated dizziness symptoms, only 0.7% were on a cerebrovascular basis.[8] Isolated vertigo often indicates a peripheral vestibular disturbance—the most common cause of brief positional vertigo attacks (lasting a few seconds) is benign paroxysmal positional vertigo, which can be cured by a bedside repositioning maneuver (*e.g.*, Epley maneuver). Acute vertigo that is suggestive of a vertebrobasilar ischemic event is usually accompanied by other neurological features, particularly gait imbalance or ataxia, limb incoordination, double vision or slurred speech.

Migraine visual aura is frequently mistaken for TIA, especially when it is not accompanied by headache (sometimes referred to as "acephalgic migraine," "complicated migraine," or "migraine equivalents"). The clue to migraine aura is the presence of positive scotomata (a visual hallucination often with jagged, scintillating lines, waves, or vivid colours with or without a negative central scotoma) and it is characteristically a binocular rather than a monocular disturbance. Patients should see the visual imagery when covering each eye separately and with both eyes closed.

Somatosensory migraine auras are characterized by paresthesias that progress from one body part to another over time (*e.g.*, pins and needles sensation in the fingers of one hand that travel up the arm and then into the mouth and face). Occasionally, a mild transient Broca's type aphasic disturbance occurs as part of a migrainous aura; these are often difficult to distinguish from a true TIA. Additional TIA mimics include focal epileptic seizures, symptoms related to brain tumour or subdural hematoma, metabolic disturbances, dementia, delirium, psychogenic disorders and peripheral neuropathy (*e.g.*, carpal tunnel syndrome, ulnar nerve irritation, cervical nerve root pathology, sciatica), among others.

Beatrice's case cont'd...

- Beatrice is diagnosed with an acute transient left cerebral ischemic event due to symptomatic high-grade carotid artery stenosis
- She undergoes definitive treatment with carotid endarterectomy on an urgent basis
- Medical treatment involves antiplatelet therapy, a statin and antihypertensive therapy
- She remains asymptomatic and well 2 years later

The importance of identifying the underlying cause

TIA is not a final diagnosis. There are many possible causes for TIA/stroke symptoms. For a practical etiological classification, we recommend using the Trial of ORG 10172 in the Acute Stroke Treatment (TOAST) criteria[9] (Table 2). The etiological diagnosis has implications for prognosis and urgency of assessment and is a prerequisite for prescribing the correct therapies for secondary prevention.

In terms of the risk of early stroke recurrence, symptomatic patients with large artery atherosclerosis (*i.e.*, carotid or vertebrobasilar occlusive disease) have a higher risk compared to patients with TIA/stroke due to other causes. According to a meta-analysis, the three-month risk of recurrent stroke following a TIA or ischemic stroke was 19% when the mechanism was large-artery atherosclerotic disease, 12% for cardiogenic brain

Table 2

Practical etiological classification for TIA/ischemic stroke and implications for prognosis and treatment

TOAST etiological classification[9]	3-month risk of recurrent stroke[10]	Main treatment options to consider for secondary stroke prevention*
1. Large-artery atherosclerosis (*i.e.*, extracranial or intracranial occlusive disease of carotid or vertebrobasilar systems)	19%	Carotid revascularization, antihypertensive therapy, antiplatelet therapy, lipid lowering therapy
2. Small-artery (lacunar) disease	3%	Antihypertensive therapy, Antiplatelet therapy
3. Cardioembolism	12%	Anticoagulation for AF, atrial flutter, mechanical heart valves and selected other cardiac conditions
4. Undetermined etiology - diagnostic evaluation complete - diagnostic evaluation incomplete	9%	Antiplatelet therapy
5. Other determined cause	N/A	Depends on the specific cause

TOAST: Trial of ORG 10172 in the Acute Stroke Treatment * General risk factor modification applies to all patients

embolism, 9% for those of unknown etiology and 3% for small-vessel strokes.[10]

Risk for patients with a TIA due to carotid artery stenosis

Patients with a cerebral ischemic event due to symptomatic carotid artery disease (50% to 99% stenosis) represent a high-risk subgroup. The 30-day risk of recurrent stroke in such patients (without surgery) was 30% in the OXford VASCular study[11] (OXVASC) and the 90-day stroke risk was 20% in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) cohort.[4] Because of this early risk, there is a need to rapidly rule in or rule out the presence of significant carotid artery disease for all patients who present with symptoms compatible with a carotid-territory TIA or stroke event.

Initial diagnostic tests

The most important test to perform quickly is imaging of the carotid arteries in the neck for patients presenting clinically with an acute carotid-territory ischemic event. This can be accomplished non-invasively with carotid Doppler ultrasound, magnetic resonance angiography (MRA), or computed tomographic angiography (CTA). Such imaging should ideally be performed within 24 hours of the clinical event according to recent guidelines.[12,13] At some hospitals, CTA or MRA have become the test of choice for rapid vascular imaging, particularly on weekends or after-hours when ultrasound is usually unavailable. Unfortunately in practice, carotid imaging is often delayed. A study from Ontario hospitals in 2000 found that < 50% of patients with an ED diagnosis of TIA obtained carotid ultrasound within *one month* of presentation.[5]

Brain imaging, usually with a non-contrast CT scan, is indicated to exclude hemorrhage, tumour, or other structural pathology that may produce stroke-like symptoms; it may also reveal the presence of acute or chronic infarcts. However, the brain imaging test of choice for TIA patients, where available, is a MRI scan.

Routine bloodwork should be obtained, plus a fasting lipid profile, fasting glucose and hemoglobin A1C. A 12-lead EKG should be performed to screen for atrial fibrillation (AF) or other high-risk cardiac sources of emboli.

Echocardiography and Holter monitor studies are usually reserved for patients in whom the initial diagnostic evaluation is unremarkable or when a cardioembolic mechanism is suspected (*e.g.*, cortical infarcts or an imaging pattern of multiple acute emboli in different vascular territories). In a patient presenting with an unexplained TIA, it is important to screen for the possibility of paroxysmal AF, particularly in the absence of any significant large vessel atherosclerotic disease.

How can a MRI scan help?

A diffusion-weighted (DW) MRI scan is the most sensitive and specific test for detecting the presence of acute cerebral ischemia; it is particularly helpful in confirming the clinical diagnosis of a suspected acute ischemic event in patients whose symptoms have cleared and when the neurological examination is normal.

In many cases, a MRI scan shows that the TIA is really a small stroke whose symptoms were transient. To be most informative, DW MRI scans need to be performed *within the first few days* post TIA. After several days, the diffusion abnormalities will vanish. Therefore, if a MRI scan is obtained too late, it may no longer be possible to confirm whether or not the patient's presenting symptoms represented a true acute cerebral ischemic event.

The pattern of imaging abnormalities is also informative (*e.g.*, a DW MRI scan that shows multiple simultaneous bilateral cerebral lesions is strongly suspicious for cardiogenic brain embolism and should direct investigations toward the identification of AF, another cardiac cause, or aortic arch atheroma). Furthermore, a DW MRI scan is also a strong risk stratification tool for predicting stroke risk after TIA. For example, if the DW MRI scan demonstrates acute cerebral ischemia, the risk of stroke recurrence is increased four- to five-fold. The presence of multiple, rather than single, DW lesions also predicts greater stroke risk. In some hospitals, a MRI scan is available in the ED to assist with triage decisions for patients with a suspected acute TIA or minor stroke.[14]

A MRI scan is the most sensitive and specific test for detecting the presence of acute cerebral ischemia.

Occasionally, a MRI scan will reveal that the TIA was caused not by ischemia, but rather by a cerebral microhemorrhage (*i.e.*, a small microbleed that is detectable on gradient-echo MRI scan but is too small to be visible on a routine CT scan).

Importantly, MRI also frequently reveals evidence of chronic asymptomatic cerebrovascular disease (*e.g.*, prior "silent strokes" [ischemic or hemorrhagic], which are important to recognize since such findings predict an increased risk for future clinical strokes and dementia).

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For references, please contact **cme@sta.ca**

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